Qeios

Peer Review

Review of: "Long-Term Risk of Medication-Related Osteonecrosis of the Jaw (MRONJ) After Bisphosphonates and/or Denosumab in Metastatic Breast Cancer Patients"

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The risk of osteonecrosis secondary to denosumab therapy (60 mg or 120 mg) has been known in the literature since the drug's introduction in 2010 in cancer therapies. Wong et al. in 2012 (1) wrote that "ONJ was reported at similar rates for patients on denosumab compared to zoledronic acid."

Probably, the correlation between some dental diseases and surgical procedures, denosumab, and the occurrence of ONJ was not known to oncologists and dentists during the whole period reviewed by Brunner et al. (2).

Brunner et al. (2) make no assessment of the existence of a dental protocol put in place prior to the prescription of denosumab, zoledronic acid, or both.

It is unclear, neither in Brunner et al. (2) nor in Fusco et al. (3), what the real cause of ONJs is: the drug itself, or a faulty dental procedure resulting from the lack of knowledge of the specific problem on the part of oncologic and dental caregivers at the time of administration, in particular for those patients who received the therapy in the early 2000s or 2010 for BPs and denosumab, respectively?

The observation period from 2000 to 2020 in this retrospective study may have the problem of a lack of knowledge of the risk of ONJ associated with denosumab and invasive dental procedures by the dentist. As reported also by Fusco et al. (3), it would be interesting to analyze the data by differentiating the observations according to the timing of treatments (2000-2005; 2005-2010; 2010-2015; 2015-2020). Brunner et al.'s conclusion that "the study revealed significantly higher incidence

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rates of MRONJ than most of the international literature" may change, possibly observing a reduction in ONJ incidence as time increases since denosumab was first introduced into cancer therapies. In fact, a higher awareness of the relation between dental state/procedures and ONJ has recently spread among dentists, oncologists, and patients.

A PUBMED search (performed on Jan. 05, 2024) for "incidence" "onj" "denosumab," choosing a custom range of publication dates for the period 2000-2005, gave no results; for 2005-2010, no results; for 2010-2015, 16 results; for 2015-2020, 33 results; and for 2020-2025, 21 results.

Considering the published literature from 2020 to 2025, variable incidence values of denosumab-associated ONJ are found, e.g., 28.3 per 10,000 observed patient-years (4) or 1.47 per 1,000 person-years (5) or 3.0 per 100 person-years (6).

Considering these factors, the reported high incidence of ONJ linked to denosumab, compared with other data in recent literature, should be critically reviewed and approached with caution.

References

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Declarations

Potential competing interests: No potential competing interests to declare.